Response to Letter by Hamilton et al

The point raised by Hamilton et al is well taken. We apologize for not referring to their 2008 study showing a PKG-dependent NPR-C–coupled nitric oxide synthase (NOS) activation in rabbit ventricular myocytes that leads to soluble guanylyl cyclase (sGC) activation. Although their study is relevant to our recent study published in Circulation Research, we do not believe that activation via atrial natriuretic peptide (ANP) of sGC interferes with our cGMP measurements. Indeed, if part of the cGMP response to ANP was attributable to NO-dependent sGC activation, it should share some common features with the cGMP response produced by NO donors. However, this was not the case. First, as shown in our 2 studies, ANP or BNP induced a clear activation of the subsarcolemmal cGMP concentration (as evidenced by the cGMP-gated current, $I_{CNG}$) whereas NO donors had little effect. Second, the PDE5 inhibitor sildenafil produced a strong increase of $I_{CNG}$ activated by NO donors but had no effect on the current elicited by ANP. Finally, adding an NO donor (SNAP) on top of a nonmaximal concentration of ANP did not produce additional increase in subsarcolemmal cGMP concentration. This indicates that ANP and NO activate different pools of cGMP in adult rat ventricular myocytes and that ANP does not activate sGC. The difference between our results and those of William et al may be attributable to species differences.

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Disclosures

None.

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